

What is claimed is:

1. A method of producing a cloned non-human mammalian NT embryo, the method comprising introducing donor genetic material into a metaphase I oocyte to yield a cloned non-human mammalian NT embryo.
2. The method of claim 1 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is at metaphase.
3. The method of claim 2 further comprising arresting the donor cell at metaphase by exposure of the donor cell to an arresting agent.
4. The method of claim 1 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is arrested at late G1 phase.
5. The method of claim 1 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is proliferating.
6. The method of claim 1 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is quiescent.
7. The method of claim 1 wherein the donor genetic material introduced into the oocyte comprises an isolated nucleus.
8. The method of claim 1 wherein the donor genetic material introduced into the oocyte comprises an isolated metaphase plate.
9. The method of claim 1 wherein the donor genetic material introduced into the oocyte is present in a donor cell.
10. The method of claim 9 further comprising fusing the donor cell and the oocyte.

11. The method of claim 1 wherein the donor genetic material introduced into the oocyte is obtained from a differentiated cell.
12. The method of claim 11 wherein the differentiated cell is selected from the group consisting of a fibroblast, an epithelial cell, a hematopoietic cell, and a lymphocyte.
13. The method of claim 12 wherein the epithelial cell is a cumulus cell.
14. The method of claim 11 wherein the differentiated cell is obtained from a source selected from the group consisting of a late embryogenic stage embryo, a fetus, an adult, and a cultured cell line.
15. The method of claim 1 further comprising activating the oocyte or the NT embryo.
16. The method of claim 15 wherein activating the oocyte occurs before the donor genetic material is introduced into the oocyte.
17. The method of claim 15 wherein activating the oocyte or the NT embryo occurs at about the same time the donor genetic material is introduced into the oocyte.
18. The method of claim 15 wherein activating the NT embryo occurs after the donor genetic material is introduced into the oocyte.
19. The method of claim 1 further comprising enucleating the oocyte before introducing the donor genetic material.
20. The method of claim 1 further comprising enucleating the NT embryo after introducing the donor genetic material to the oocyte, wherein enucleating

the NT embryo comprises removal of maternal genetic material.

21. The method of claim 1 wherein the oocyte is arrested at metaphase I as a result of exposure to an arresting agent.

22. The method of claim 19 wherein the oocyte is enucleated while in metaphase I.

23. The method of claim 1 wherein the donor genetic material comprises transgenic DNA.

24. The method of claim 15 wherein activating comprises introducing to the oocyte or the NT embryo cytoplasm from a fertilized oocyte.

25. The method of claim 15 wherein activating comprises artificially activating the oocyte or the NT embryo.

26. The method of claim 25 wherein activating comprises using cycloheximide.

27. The cloned non-human mammalian NT embryo of claim 1.

28. The method of claim 1 wherein the non-human mammal is a pig or a cow.

29. A method of producing a cloned pig NT embryo, the method comprising introducing donor genetic material into a metaphase I oocyte to yield a cloned non-human mammalian NT embryo.

30. A method of producing a cloned pig NT embryo, the method comprising introducing donor genetic material into an oocyte to yield a cloned non-human mammalian NT embryo, wherein the donor genetic material is obtained from an

adult fibroblast.

31. A method of producing a cloned pig NT embryo, the method comprising introducing donor genetic material into a metaphase I oocyte to yield a cloned non-human mammalian NT embryo, wherein the donor genetic material is obtained from an adult fibroblast.

32. A method of producing a cloned pig NT embryo, the method comprising introducing donor genetic material into a metaphase II oocyte to yield a cloned non-human mammalian NT embryo, wherein the donor genetic material is obtained from an adult fibroblast.

33. A method of producing a cloned non-human mammal comprising:
incubating a mammalian NT embryo such that the NT embryo undergoes cell division, wherein the NT embryo is produced by introducing donor genetic material into a metaphase I oocyte to yield a cloned non-human mammal.

34. The method of claim 33 wherein incubating the NT embryo occurs after transfer of the NT embryo to a host mammal.

35. The method of claim 33 wherein incubating the NT embryo comprises culturing the NT embryo *in vitro* until at least the 2-cell stage.

36. The method of claim 35 further comprising transferring the NT embryo to a host mammal after the *in vitro* incubation.

37. The cloned non-human mammal of claim 33.

38. The method of claim 36 wherein the NT embryo undergoes cell division in the host mammal and develops into a fetus.

39. The method of claim 36 wherein the NT embryo undergoes cell division in the host mammal and develops into an offspring.
40. The fetus of claim 38.
41. The offspring of claim 39.
42. The method of claim 33 wherein the non-human mammal is a pig or a cow.
43. A method of producing a cloned pig comprising:
incubating a pig NT embryo such that the NT embryo undergoes cell division, wherein the NT embryo is produced by introducing donor genetic material into a metaphase I oocyte to yield a cloned pig.
44. A method of producing a cloned pig comprising:
incubating a pig NT embryo such that the NT embryo undergoes cell division, wherein the NT embryo is produced by introducing donor genetic material into an oocyte to yield a cloned pig, and wherein the donor genetic material is obtained from an adult fibroblast.
45. A method of producing a cloned pig comprising:
incubating a pig NT embryo such that the NT embryo undergoes cell division, wherein the NT embryo is produced by introducing donor genetic material into a metaphase I oocyte to yield a cloned pig, and wherein the donor genetic material is obtained from an adult fibroblast.
46. A method of producing a cloned pig comprising:

incubating a pig NT embryo such that the NT embryo undergoes cell division, wherein the NT embryo is produced by introducing donor genetic material into a metaphase II oocyte to yield a cloned pig, and wherein the donor genetic material is obtained from an adult fibroblast.

47. A method of producing a cloned non-human mammalian NT embryo, the method comprising introducing donor genetic material into a non-enucleated oocyte to yield a cloned non-human mammalian NT embryo.

48. The method of claim 47 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is at metaphase.

49. The method of claim 48 further comprising arresting the donor cell at metaphase by exposure of the donor cell to an arresting agent.

50. The method of claim 47 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is arrested at late G1 phase.

51. The method of claim 47 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is proliferating.

52. The method of claim 47 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is quiescent.

53. The method of claim 47 wherein the donor genetic material introduced into the oocyte comprises an isolated nucleus.

54. The method of claim 47 wherein the donor genetic material introduced into the oocyte comprises an isolated metaphase plate.

55. The method of claim 47 wherein the donor genetic material introduced

into the oocyte is present in a donor cell.

56. The method of claim 55 further comprising fusing the donor cell and the oocyte.

57. The method of claim 47 wherein the donor genetic material introduced into the oocyte is from a differentiated cell.

58. The method of claim 57 wherein the differentiated cell is selected from the group consisting of a fibroblast, an epithelial cell, a hematopoietic cell, and a lymphocyte.

59. The method of claim 58 wherein the epithelial cell is a cumulus cell.

60. The method of claim 57 wherein the differentiated cell is obtained from a source selected from the group consisting of a late embryogenic stage embryo, a fetus, an adult, and a cultured cell line.

61. The method of claim 47 further comprising activating the oocyte or the NT embryo.

62. The method of claim 61 wherein activating the oocyte occurs before the donor genetic material is introduced into the oocyte.

63. The method of claim 61 wherein activating the oocyte or NT embryo occurs at about the same time the donor genetic material is introduced into the oocyte.

64. The method of claim 61 wherein activating the NT embryo occurs after the donor genetic material is introduced into the oocyte.

65. The method of claim 47 further comprising enucleating the NT embryo

after introducing the donor genetic material to the oocyte, wherein enucleating the NT embryo comprises removal of maternal genetic material.

66. The method of claim 47 wherein the oocyte is in metaphase I.
67. The method of claim 66 wherein the oocyte is arrested at metaphase I as a result of exposure to an arresting agent.
68. The method of claim 47 wherein the donor genetic material comprises transgenic DNA.
69. The method of claim 61 wherein activating comprises introducing to the oocyte or the NT embryo cytoplasm from a fertilized oocyte.
70. The method of claim 61 wherein activating comprises artificially activating the oocyte or the NT embryo.
71. The method of claim 70 wherein activating comprises using cycloheximide.
72. The cloned non-human mammalian NT embryo of claim 47.
73. The method of claim 47 wherein the non-human mammal is a pig or a cow.
74. A method of producing a cloned non-human mammal comprising:
incubating a mammalian NT embryo such that the NT embryo undergoes
cell division to yield a cloned non-human mammal, wherein the
NT embryo is produced by introducing donor genetic material
into a non-enucleated oocyte.
75. The method of claim 74 wherein incubating the NT embryo occurs after

transfer of the NT embryo to a host mammal.

76. The method of claim 74 wherein incubating the NT embryo comprises culturing the NT embryo *in vitro* until at least the 2-cell stage.

77. The method of claim 76 further comprising transferring the NT embryo to a host mammal after the *in vitro* incubation.

78. The method of claim 77 wherein the NT embryo undergoes cell division in the host mammal and develops into a fetus.

79. The method of claim 77 wherein the NT embryo undergoes cell division in the host mammal and develops into an offspring.

80. The fetus of claim 78.

81. The offspring of claim 79.

82. The cloned non-human mammal of claim 74.

83. The method of claim 74 wherein the non-human mammal is a pig or a cow.

84. A method of producing a cloned non-human mammalian NT embryo, the method comprising introducing donor genetic material obtained from a donor cell that is at metaphase into an oocyte to yield a cloned non-human NT embryo.

85. The method of claim 84 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is at metaphase as a result of exposure to an arresting agent.

86. The method of claim 84 wherein the donor genetic material introduced

into the oocyte is obtained from a donor cell that is proliferating.

87. The method of claim 84 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is quiescent.

88. The method of claim 84 wherein the donor genetic material introduced into the oocyte comprises an isolated nucleus.

89. The method of claim 84 wherein the donor genetic material introduced into the oocyte comprises an isolated metaphase plate.

90. The method of claim 84 wherein the donor genetic material introduced into the oocyte is present in a donor cell.

91. The method of claim 90 further comprising fusing the donor cell and the oocyte.

92. The method of claim 84 wherein the donor genetic material introduced into the oocyte is from a differentiated cell.

93. The method of claim 92 wherein the differentiated cell is selected from the group consisting of a fibroblast, an epithelial cell, a hematopoietic cell, and a lymphocyte.

94. The method of claim 93 wherein the epithelial cell is a cumulus cell.

95. The method of claim 92 wherein the differentiated cell is obtained from a source selected from the group consisting of a late embryogenic stage embryo, a fetus, an adult, and a cultured cell line.

96. The method of claim 84 further comprising activating the oocyte or the NT embryo.

97. The method of claim 96 wherein activating the oocyte occurs before the donor genetic material is introduced into the oocyte.

98. The method of claim 96 wherein activating the oocyte or the NT embryo occurs at about the same time the donor genetic material is introduced into the oocyte.

99. The method of claim 96 wherein activating the NT embryo occurs after the donor genetic material is introduced into the oocyte.

100. The method of claim 84 further comprising enucleating the oocyte before introducing the donor genetic material.

101. The method of claim 84 further comprising enucleating the NT embryo after introducing the donor genetic material to the oocyte, wherein enucleating the NT embryo comprises removal of maternal genetic material.

102. The method of claim 84 wherein the oocyte is arrested at metaphase I as a result of exposure to an arresting agent.

103. The method of claim 84 wherein the oocyte is enucleated while in metaphase I.

104. The method of claim 84 wherein the donor genetic material comprises transgenic DNA.

105. The method of claim 96 wherein activating comprises introducing to the oocyte or the NT embryo cytoplasm from a fertilized oocyte.

106. The method of claim 96 wherein oocyte or NT embryo is artificially activated.

107. The method of claim 106 wherein activating comprises using cycloheximide.
108. The cloned non-human mammal NT embryo of claim 84.
109. The method of claim 84 wherein the non-human mammal is a pig or a cow.
110. A method of producing a cloned non-human mammal comprising:
incubating a mammalian NT embryo such that the NT embryo undergoes cell division to yield a cloned non-human mammal, wherein the NT embryo is produced by introducing donor genetic material obtained from a donor cell that is at metaphase into an oocyte.
111. The method of claim 110 wherein incubating the NT embryo occurs after transfer of the activated NT embryo to a host mammal.
112. The method of claim 110 wherein incubating the NT embryo comprises culturing the activated NT embryo *in vitro* until at least the 2-cell stage.
113. The method of claim 112 further comprising transferring the NT embryo to a host mammal after the *in vitro* incubation.
114. The method of claim 113 wherein the NT embryo undergoes cell division in the host mammal and develops into a fetus.
115. The method of claim 113 wherein the NT embryo undergoes cell division in the host mammal and develops into an offspring.
116. The fetus of claim 114.

117. The offspring of claim 115.

118. The cloned non-human mammal of claim 110.

119. The method of claim 110 wherein the non-human mammal is a pig or a cow.

120. A method of producing a cloned non-human mammalian NT embryo, the method comprising introducing donor genetic material into an oocyte to yield a cloned non-human mammalian NT embryo, and naturally activating the oocyte or the NT embryo.

121. The method of claim 120 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is at metaphase.

122. The method of claim 121 further comprising arresting the donor cell at metaphase by exposure of the donor cell to an arresting agent.

123. The method of claim 120 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is arrested at late G1 phase.

124. The method of claim 120 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is proliferating.

125. The method of claim 120 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is quiescent.

126. The method of claim 120 wherein the donor genetic material introduced into the oocyte comprises an isolated nucleus.

127. The method of claim 120 wherein the donor genetic material introduced into the oocyte comprises an isolated metaphase plate.

128. The method of claim 120 wherein the donor genetic material introduced into the oocyte is present in a donor cell.

129. The method of claim 128 further comprising fusing the donor cell and the oocyte.

130. The method of claim 120 wherein the donor genetic material introduced into the oocyte is from a differentiated cell.

131. The method of claim 130 wherein the differentiated cell is selected from the group consisting of a fibroblast, an epithelial cell, a hematopoietic cell, and a lymphocyte.

132. The method of claim 131 wherein the epithelial cell is a cumulus cell.

133. The method of claim 130 wherein the differentiated cell is obtained from a source selected from the group consisting of a late embryogenic stage embryo, a fetus, an adult, and a cultured cell line.

134. The method of claim 120 wherein naturally activating the oocyte occurs before the donor genetic material is introduced into the oocyte.

135. The method of claim 120 wherein naturally activating the oocyte or the NT embryo occurs at about the same time the donor genetic material is introduced into the oocyte.

136. The method of claim 120 wherein naturally activating the NT embryo occurs after the donor genetic material is introduced into the oocyte.

137. The method of claim 120 wherein naturally activating comprises adding to the oocyte or the NT embryo cytoplasm obtained from a fertilized oocyte.

138. The method of claim 120 wherein naturally activating comprises removing the donor genetic material from the NT embryo and introducing the donor genetic material to an enucleated fertilized oocyte.

139. The method of claim 120 further comprising enucleating the oocyte before introducing the donor genetic material.

140. The method of claim 120 further comprising enucleating the NT embryo after introducing the donor genetic material to the oocyte, wherein enucleating the NT embryo comprises removal of maternal genetic material.

141. The method of claim 120 wherein the oocyte is arrested at metaphase I as a result of exposure to an arresting agent.

142. The method of claim 139 wherein the oocyte is enucleated while in metaphase I.

143. The method of claim 120 wherein the donor genetic material comprises transgenic DNA.

144. The method of claim 120 wherein activation comprises using cytoplasm from a fertilized oocyte.

145. The cloned non-human mammalian NT embryo of claim 120.

146. The method of claim 120 wherein the non-human mammal is a pig or a cow.

147. A method of producing a cloned non-human mammal comprising:
incubating a mammalian NT embryo such that the NT embryo undergoes
cell division to yield a cloned non-human mammal, wherein the

NT embryo is produced by introducing donor genetic material into an oocyte, and wherein the oocyte of the NT embryo is naturally activated.

148. The method of claim 147 wherein incubating the NT embryo occurs after transfer of the activated NT embryo to a host mammal.

149. The method of claim 147 wherein incubating the NT embryo comprises culturing the activated NT embryo *in vitro* until at least the 2-cell stage.

150. The method of claim 149 further comprising transferring the NT embryo to a host mammal after the *in vitro* incubation.

151. The method of claim 150 wherein the NT embryo undergoes cell division in the host mammal and develops into a fetus.

152. The method of claim 150 wherein the NT embryo undergoes cell division in the host mammal and develops into an offspring.

153. The fetus of claim 151.

154. The offspring of claim 152.

155. The cloned non-human mammal of claim 147.

156. The method of claim 147 wherein the non-human mammal is a pig or a cow.

157. A method of producing a cloned non-human mammalian NT embryo, the method comprising introducing donor genetic material obtained from a donor cell that is at late G1 phase into an oocyte to yield a cloned non-human NT embryo.

158. The method of claim 157 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is at late G1 phase as a result of exposure to an arresting agent.

159. The method of claim 157 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is proliferating.

160. The method of claim 157 wherein the donor genetic material introduced into the oocyte is obtained from a donor cell that is quiescent.

161. The method of claim 157 wherein the donor genetic material introduced into the oocyte comprises an isolated nucleus.

162. The method of claim 157 wherein the donor genetic material introduced into the oocyte is present in a donor cell.

163. The method of claim 162 further comprising fusing the donor cell and the oocyte.

164. The method of claim 157 wherein the donor genetic material introduced into the oocyte is from a differentiated cell.

165. The method of claim 164 wherein the differentiated cell is selected from the group consisting of a fibroblast, an epithelial cell, a hematopoietic cell, and a lymphocyte.

166. The method of claim 165 wherein the epithelial cell is a cumulus cell.

167. The method of claim 154 wherein the differentiated cell is obtained from a source selected from the group consisting of a late embryogenic stage embryo, a fetus, an adult, and a cultured cell line.

168. The method of claim 157 further comprising activating the oocyte or the NT embryo.

169. The method of claim 168 wherein activating the oocyte occurs before the donor genetic material is introduced into the oocyte.

170. The method of claim 168 wherein activating the oocyte or the NT embryo occurs at about the same time the donor genetic material is introduced into the oocyte.

171. The method of claim 168 wherein activating the NT embryo occurs after the donor genetic material is introduced into the oocyte.

172. The method of claim 157 further comprising enucleating the oocyte before introducing the donor genetic material.

173. The method of claim 157 further comprising enucleating the NT embryo after introducing the donor genetic material to the oocyte, wherein enucleating the NT embryo comprises removal of maternal genetic material.

174. The method of claim 157 wherein the oocyte is arrested at metaphase I as a result of exposure to an arresting agent.

175. The method of claim 157 wherein the oocyte is enucleated while in metaphase I.

176. The method of claim 157 wherein the donor genetic material comprises transgenic DNA.

177. The method of claim 168 wherein activating comprises introducing to the oocyte or the NT embryo cytoplasm from a fertilized oocyte.

178. The method of claim 168 wherein activating comprises artificially activating the oocyte or the NT embryo.
179. The method of claim 178 wherein activating comprises using cycloheximide.
180. The cloned non-human mammalian NT embryo of claim 157.
181. The method of claim 157 wherein the non-human mammal is a pig or a cow.
182. A method of producing a cloned non-human mammal comprising:
incubating a mammalian NT embryo such that the NT embryo undergoes cell division to yield a cloned non-human mammal, wherein the NT embryo is produced by introducing donor genetic material obtained from a donor cell that is at late G1 phase into an oocyte to yield a cloned non-human NT embryo.
183. The method of claim 182 wherein incubating the NT embryo occurs after transfer of the activated NT embryo to a host mammal.
184. The method of claim 182 wherein incubating the NT embryo comprises culturing the activated NT embryo *in vitro* until at least the 2-cell stage.
185. The method of claim 184 further comprising transferring the NT embryo to a host mammal after the *in vitro* incubation.
186. The method of claim 185 wherein the NT embryo undergoes cell division in the host mammal and develops into a fetus.
187. The method of claim 185 wherein the NT embryo undergoes cell division

in the host mammal and develops into an offspring.

188. The fetus of claim 186.

189. The offspring of claim 187.

190. The cloned non-human mammal of claim 182.

191. The method of claim 182 wherein the non-human mammal is a pig or a cow.

192. A method of producing a cloned cow NT embryo, the method comprising introducing donor genetic material obtained from a donor cell that is arrested at late G1 phase into an oocyte to yield a cloned cow NT embryo.

193. A method of producing a cloned cow NT embryo, the method comprising introducing donor genetic material obtained from a donor cell that is arrested at late G1 phase into an oocyte to yield a cloned cow NT embryo, wherein the donor cell is arrested at late G1 phase by an arresting agent.

194. A method of producing a cloned cow NT embryo, the method comprising introducing donor genetic material obtained from a donor cell that is arrested at late G1 phase into an oocyte to yield a cloned cow NT embryo, wherein the donor cell is arrested at late G1 phase by an arresting agent that inhibitor CDK2 kinase.

195. A method of producing a cloned cow NT embryo, the method comprising introducing donor genetic material obtained from a donor cell that is arrested at late G1 phase into an oocyte to yield a cloned cow NT embryo, wherein the donor cell is arrested at late G1 phase by roscovitine or olomoucine.

196. A method of producing a cloned cow NT embryo, the method comprising

introducing donor genetic material obtained from a donor cell that is arrested at late G1 phase into an oocyte to yield a cloned cow NT embryo, wherein the donor cell is arrested at late G1 phase by roscovitine.